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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional)
CLFR:178USD1

I hereby certify that this correspondence is being electronically submitted to Commissioner for Patents on November 1, 2006

Signature

Typed or printed name David L. Parker

Application Number	Filed
10/695,275	October 28, 2003

First Named Inventor
Bob G. Sanders, et al.

Art Unit	Examiner
1623	Devesh Khare

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- ☐ applicant/inventor.
- ☐ assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- ☑ attorney or agent of record. Registration number 32,165.
- ☐ attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

Signature

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Telephone number

November 1, 2006
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☐ *Total of _____ forms are submitted.

This collection of information is required by 35 U.S.C. 132. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11, 1.14 and 41.6. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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Arguments in Support of Pre-Appeal Brief Request for 10/695,275

I. Regarding the Enablement Rejection[1]

The Examiner rejects Applicant's claims directed toward a "method for inhibiting the growth of tumor cells in an individual comprising administering to the individual a pharmacologically effective dose of a compound"[2] of this invention. This enablement rejection is unreasonable given that the Applicants have shown that the method of this invention does inhibit the growth of a wide variety of tumor cells. The examples and screening techniques disclosed by the Applicants are in relation to the scope of the claims based on the relative predictability of the art; therefore, the claims are enabled.

A common thread running through the arguments of this Action, as well as the arguments of the previous Actions, is that the Applicants must show that each and every compound covered by claim 1 will inhibit every possible form of cancer. This position is problematic because it applies an incorrect legal standard to the enablement requirement, and it ignores the specification of the Application and the Inventors' Declaration.[3] Both highlight the wide variety of cancer cells whose growth has been inhibited by the method of this invention. Routine screening, not undue experimentation, is all that a skilled artisan would need to do in order to test the applicability of this invention to other tumor cells.[4]

A variety of the compounds of this invention (chroman derivatives) were shown to induce apoptosis in one or more of the tumor cell lines. These examples were summarized in Tables 2 – 3 on pages 95 – 98 of the application. These tables are reproduced here:

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[1] Action of August 1, 2006, pages 3-6.
[2] *See* claim 1 of Application.
[3] "Declaration of Bob G. Sanders, Ph.D. and Kimberly Kline, Ph.D., under 37 C.F.R. §1.132", November, 28, 2005.
[4] Enablement is not precluded by the necessity for some experimentation such as routine screening. In re Wands, 858 F.2d 731, 736-37 (Fed. Cir. 1988).

Table 2-1

Cell Type	VES	1	2	3	4	5	6	7
Breast Cancer								
HMEC	N	N	N	N	N	N	N	N
MCF-10A	N	N	N	N	N	N	N	N
MDA-MB-435	5-10	5-10	10-20	5-10	N	N	N	5-10
MDA-MB-231	5-10	5-10	10-20	5-10	N	N	N	5-10
MCF-7	10-20	5-10	20-30	20-30	N	N	N	10-20
T47D	N	N	N	N	N	N	N	N
Cervical								
ME-180	10-20	1-5	5-10	10-20	N	N	N	5-10
Ovarian								
C-170	N	10-20	10-20	10-20	N	N	N	10-20
Endomerial								
RL-95-2	10-20	10-20	10-209	10-20	N	N	N	5-10
Prostate								
PREC	N	N	NT	NT	NT	NT	NT	NT
LnCaP	5-10	5-10	5-10	5-10	N	N	N	2.5-5
PC-3	10-20	5-10	5-10	5-10	N	N	N	5-10
DU-145	10-20	5-10	NT	NT	NT	NT	NT	NT
Colon								
HT-29	5-10	10-20	NT	NT	NT	NT	NT	NT
DLD-1	10-20	10-20	NT	NT	NT	NT	NT	NT
Lung								
A-549	20-30	10-20	NT	NT	NT	NT	NT	NT
Lymphoid Cells								
Myeloma	10-20	NT	NT	NT	NT	NT	NT	NT
Raji	10-20	NT	NT	NT	NT	NT	NT	NT
Ramos	10-20	NT	NT	NT	NT	NT	NT	NT
Jurkat	10-20	10-20	NT	NT	NT	NT	NT	NT
HL-60	10-20	5-10	10-20	10-20	N	N	N	5-10

Table 2-2

Cell Type	8	9	10	11	12	13	14	15
Breast Cancer								
HMEC	N	N	N	N	N	N	N	NT
MCF-10A	N	N	N	N	N	N	N	NT
MDA-MB-435	5-10	5-10	N	N	5-10	N	N	20-30
MDA-MB-231	5-10	5-10	N	N	5-10	N	N	20-30
MCF-7	10-20	10-20	N	N	5-10	N	N	20-30
T47D	NT	NT	NT	NT	NT	NT	NT	NT
Cervical								
ME-180	5-10	5-10	N	N	5-10	N	N	N
Ovarian								
C-170	10-20	N	N	N	10-20	N	N	N
Endomerial								
RL-95-2	1-5	5-10	N	N	5-10	N	N	N
Prostate								
PREC	NT	NT	NT	NT	NT	NT	NT	NT
LnCaP	5-10	5-10	N	N	>20-30	NT	N	NT
PC-3	5-10	5-10	NT	N	10-20	N	N	NT
DU-145	NT	NT	NT	NT	NT	NT	NT	NT
Colon								
HT-29	NT	NT	NT	NT	NT	NT	NT	NT
DLD-1	NT	NT	NT	NT	NT	NT	NT	NT
Lung								
A-549	NT	NT	NT	NT	NT	NT	NT	NT
Lymphoid Cells								
Myeloma	NT	NT	NT	NT	NT	NT	NT	NT
Raji	NT	NT	NT	NT	NT	NT	NT	NT
Ramos	NT	NT	NT	NT	NT	NT	NT	NT
Jurkat	NT	NT	NT	NT	NT	NT	NT	NT
HL-60	10-20	10-20	N	N	20-30	N	N	NT

Table 3-1

Cell Type	16	17	18	19	20	21	22	23
Breast Cancer								
HMEC	NT	NT	NT	NT	NT	NT	NT	NT
MCF-10A	NT	N	NT	N	N	N	NT	N
MDA-MB-435	N	NT	N	10-20	10-20	N	NT	N
MDA-MB-231	N	NT	NT	NT	NT	NT	NT	NT
MCF-7	N	10-20	N	10-20	5-10	N	15-20	N
T47D	NT	10-20	NT	N	5-10	NT	NT	NT
Cervical								
ME-180	NT	20-30	N	1-5	1-5	1-5	NT	NT
Ovarian								
C-170	NT	20-30	N	1-5	*	N	NT	NT
Endomerial								
RL-95-2	NT	NT	NT	NT	NT	N	NT	NT
Prostate								
PREC	NT	NT	N	NT	NT	NT	NT	NT
LnCaP	NT	10-20	NT	5-10	5-10*	N	NT	NT
PC-3	NT	NT	NT	N	5-10*	N	NT	N
DU-145	NT	NT	NT	5-10	5-10*	N	NT	N
Colon								
HT-29	NT	N	N	NT	NT	NT	NT	N
DLD-1	NT	NT	NT	NT	NT	NT	NT	NT
Lung								
A-549	NT	N	N	20-30	20-30	NT	NT	NT
Lymphoid Cells								
Myeloma	NT	NT	NT	NT	NT	NT	NT	NT
Raji	NT	NT	NT	NT	NT	NT	NT	NT
Ramos	NT	NT	NT	NT	NT	NT	NT	NT
Jurkat	NT	10-20	N	10-20	10-20	NT	NT	NT
HL-60	NT	10-20	N	10-20	10	NT	NT	NT

Table 3-2

Cell Type	24	25	26	27	28	29	39	42	43
Breast Cancer									
HMEC	NT	NT	NT	NT	NT	NT	NT	NT	NT
MCF-10A	NT	N	N	NT	NT	NT	NT	NT	NT
MDA-MB-435	N	N	20-40	NT	NT	NT	10-20	10-20	PPT
MDA-MB-231	NT	NT	NT	NT	NT	NT	NT	NT	NT
MCF-7	N	N	N	10-20	NT	NT	NT	NT	NT
T47D	NT	NT	N	NT	NT	NT	NT	NT	NT
Cervical									
ME-180	NT	N	*	NT	NT	NT	NT	NT	NT
Ovarian									
C-170	NT	N	20-30	NT NT	NT	NT	NT	NT	NT
Endomerial									
RL-95-2	NT	N	20-30	NT	NT	NT	NT	NT	NT
Prostate									
PREC	NT	NT	NT	NT	NT	NT	NT	NT	NT
LnCaP	N	N	10-20	10-20	NT	NT	NT	NT	NT
PC-3	N	20-30	N	NT	NT	NT	NT	NT	NT
DU-145	N	20-30	N	NT	NT	NT	NT	NT	NT
Colon									
HT-29	NT	N	N	NT	NT	NT	NT	NT	NT
DLD-1	N	N	20-40	NT	NT	NT	NT	NT	NT
Lung									
A-549	NT	NT	N	NT	NT	NT	NT	NT	NT
Lymphoid Cells									
Myeloma	NT	NT	NT	NT	NT	NT	NT	NT	NT
Raji	NT	NT	NT	NT	NT	NT	NT	NT	NT
Ramos	NT	NT	NT	NT	NT	NT	NT	NT	NT
Jurkat	NT	NT	20-30	NT	NT	NT	NT	NT	NT
HL-60	NT	NT	N	NT	NT	NT	NT	NT	NT

The tables summarize the apoptotic EC_{50} for a battery of test cancer cells for the twenty-nine novel RR-α-tocopherol compounds and two of the five 1-aza-α-tocopherol analogs of this invention. These studies indicated that a broad class of these compounds, comprising a variety of R groups are effective for arresting growth and inducing apoptosis in an equally broad variety of cancer cells. Furthermore, these studies showed that the compounds of this invention are not toxic to normal cells.

In parallel with the *in vitro* cell culture studies, the inventors further validated the effectiveness of the chroman ring compounds in studies using mouse model systems (see Example 15, page 109 – 112 of the application). The inventors have also shown that α-TEA, a model chroman ring compound, can reduce the human mammary tumor burden in mouse model systems and prevent metastasis of these cancer cells (see Table 6, page 119). In yet another example, Table 4 on page 100, the inventors showed that the amount of compound 44 needed to induce growth arrest in 50% of MDA-MB-43 tumor cells was shown to be 6 times less than the amount of compound 1 required for the same anti-proliferative activity. Applicants have therefore provided a representative group of examples of using the compounds of this invention to inhibit the growth of a diverse variety of tumor cells. These examples are in relation to the scope of the claims based on the relative predictability of the art.

The Examiner has provided no evidence that any of the claims are not enabled. Indeed, the Examiner has conceded that the claims are enabled as to:

- A "method of inducing apoptosis of a cell comprising administering an effective amount of a compound" of this invention. *See* Action of 09/10/2004, page 2.
- "[F]ifteen out of twenty nine RRR-α-tocopherol compounds and two out of five 1-aza-α-tocopherol analogs effective at inducing tumor cells to undergo apoptosis which having no apoptotic inducing properties on normal cells." *See* Action of 06/01/2005, page 2.
- "[F]or *in vitro screening* assay to determine the effective concentration of said compounds to induce apoptosis of the cells in culture." *See* Action of 03/06/2006, page 2.

Given all the aspects of the invention which the Examiner concedes are enabled, the Examiner's enablement rejection of a "method for inhibiting the growth of tumor cells in an individual

comprising administering to the individual a pharmacologically effective dose of a compound"[5] of this invention is unreasonable. The Examiner appears to confuse the requirements under the law for obtaining a patent with the requirements under the law for obtaining FDA approval to market a particular drug to the public.[6]

In view of the foregoing, it is evident that the inventors' specification provides the necessary instruction for one of skill in the art to practice the invention with the class of compounds that are claimed without undue experimentation. Based on the foregoing as well as the entire file history, it is evident that this rejection will not be sustained on appeal.

II. Regarding the 103(a) Rejection: Statement Regarding Common Ownership

The Examiner also rejected all the currently pending claims as obvious over two parent applications to which the present application claims priority, namely U.S. Patent 6,770,672 ('672) and U.S. Patent 6,417,223 ('223).[7] According to the Examiner, both of these patents constitute prior art under 35 U.S.C. 102(e). However, in so far as the '672 and '223 patents are prior art under 102(e), they also qualify for the 35 U.S.C. 103(c) exclusion. Specifically, the undersigned counsel for the Applicants avers to the fact that the present Application, as well as the '672 and '223 patents, have at all times been owned by or subject to assignment to the same party, the Board of Regents of The University of Texas System. The Action's 103(a) rejections are therefore overcome, and should be withdrawn.

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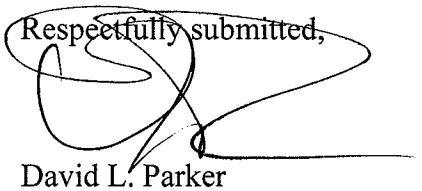
[5] *See* claim 1 of Application.
[6] *See* In re Brana, 51 F.3d 1560,1566 (Fed. Cir. 1995).
[7] Action of August 1, 2006, pages 6-9.

Respectfully submitted,



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